was 2 at ≥ 6 months follow-up. 1 DPBN-patient had G3 xerostomia at month 3 that reduced to G1 thereafter.
Conclusions; There were no local recurrences in the DPBN-group. We did not observe significant differences in LC, RC, DC or OS until now. Due to mucosal LT, the DPBN-DPP has been adapted. Since then, no G4 mucosal LT was observed. Another 66 patients will be recruited for the study.

PD-0421

HER3 pathway analysis in radiation plus concurrent cisplatin or anti-EGFR moAb for head and neck cancer

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Purpose/Objective: Concurrent cisplatin and radiation (cisp-RT) can achieve high locoregional control and survival for locally advanced head and neck cancer (LAHNC) particularly in the oropharynx, HPV+, and non-smokers. Recent retrospective reviews challenge the role of cetuximab plus radiation in this population suggesting inferior outcomes, which needs to be further confirmed. HPV negative head and neck cancer patients seem to do far worse with current strategies. This study compares concurrent cisp-RT with radiation plus anti-EGFR moAb (anti-EGFR-RT) in LAHNC in a population that is mainly HPV negative. The prognostic value of HER3 pathway-related biomarkers is explored.
Materials and Methods: From 1999 to 2010, 108 LAHNC patients with oral cavity, oropharynx, hypopharynx or larynx tumors received definitive treatment with cisp-RT (n= 71) or anti-EGFR-RT (n=37). Of these, 86 patients had tissue available for HPV analysis (PCR and p16), and 48 for HER3 pathway analysis. Outcomes were analyzed by the Kaplan-Meier method, Cox model and competing-risks analysis tools.
Results: 88% of the analyzed samples were HPV negative. Patient characteristics include 77% smokers, 70% heavy alcohol intake, 49% T4 and 69% N2-3. The anti-EGFR-RT patients were older. At a median follow-up of 4.2 years, the 2- and 5-year locoregional failure rates were 34.1% and 41.8% for cisp-RT vs 60.1% and 71.5% for anti-EGFR-RT (p=0.015). These differences remained significant for progression-free survival (p=0.0006) and were lost when distant metastasis was the only site of relapse (p=0.24). Metastasis-only relapse occurred in 14.8% of patients. In multivariate analysis, cisp-RT predicted for locoregional relapse (HR=0.53, 95%CI: 0.31-0.92, p=0.024) and progression-free survival (HR=0.44, 95%CI: 0.27-0.71, p=0.0009), whereas hypopharynx/larynx primaries (HR=5.13, 95%CI: 1.50-17.51, p=0.013) and T4 tumors (HR=2.95, 95%CI: 1.05-8.31, p=0.041) predicted for metastasis-only relapse. Subgroup analysis of HER3 pathway-related biomarkers adjusted for significant risk variables identified overexpression of pS6 (p=0.009) and p53 (p=0.049) as prognostic for locoregional failure, and pS6 (p=0.016) and HER3 (p=0.049) expression for metastasis-only relapse.
Conclusions: Superior outcomes with concurrent cisp-RT in LAHN patients are observed in a predominantly HPV negative population. It is of clinical relevance that hypopharynx/larynx primaries and T4 tumors predicted for metastasis as the only site of relapse in such a high risk group. Exploratory analyses suggest that pS6 and p53 expression predict for locoregional failure and that pS6 and HER3 do for metastasis-only relapse.

PD-0422

Validating a 2 year survival prediction model for laryngeal carcinoma patients in a clinical care and trial setting

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Purpose/Objective: Data quality of routine patients is of vital importance when creating an infrastructure for rapid learning. The aim of this work is to provide a platform that enables rapid learning for laryngeal carcinoma patients and prove the clinical relevance of a survival prediction model as a first step to multi institutional rapid learning. In this study we present a first rapid learning approach that combines learning a decision support system from MAASTRO Clinic ('training cohort') and validating it in both the Illawarra Cancer Care Centre ('clinical cohort') and the RTOG-91-11 clinical trial dataset ('trial cohort').
Materials and Methods: Data extraction and mining tools were used to collect the input parameters from the clinical cohort's OIS system (MosaiQ). The training cohort was used to determine the prognosis range for good, medium and poor prognosis patients so it could be applied to the clinical cohort and to validate the new implementation of the model. To evaluate the model performance the Area Under the Curve (AUC) spread for each dataset was calculated using bootstrapping. A similar approach was applied to the radiotherapy only arm of the trial cohort. The resulting Kaplan-Meier survival curves for the good, medium and poor prognosis groups are displayed for each separate cohort.
Results: Data mining identified 125 laryngeal carcinoma patients, resulting in 109 that were eligible to be evaluated by the model to predict 2 year survival. Bootstrapping resulted in a normally distributed AUC reliability interval (95% CI) of 0.61 to 0.84, 0.47 to 0.67 and 0.74 to 0.82 for the clinical, trial and training cohorts respectively. The predicted prognostic survival groups resulted in the Kaplan Meier curves presented in Figure 1. The survival prediction thresholds to create the poor, medium and good prognosis groups were 57% and 81% chance of 2 year survival. This resulted in a group distribution of 47%, 42% and 11% and 53%, 42% and 5% for the

poor, medium and good prognosis group for the clinical cohort and trial cohort respectively, while (by definition) the training cohort had 25%, 50% and 25% distribution. This means the model was able to classify poor and medium prognosis patients in the clinical cohort but the good prognosis patient group was very small, as the clinical cohort population was older, had more advanced cancers, more nodal spread and more non-glottic cancers which are unfavorable for the survival prognosis.

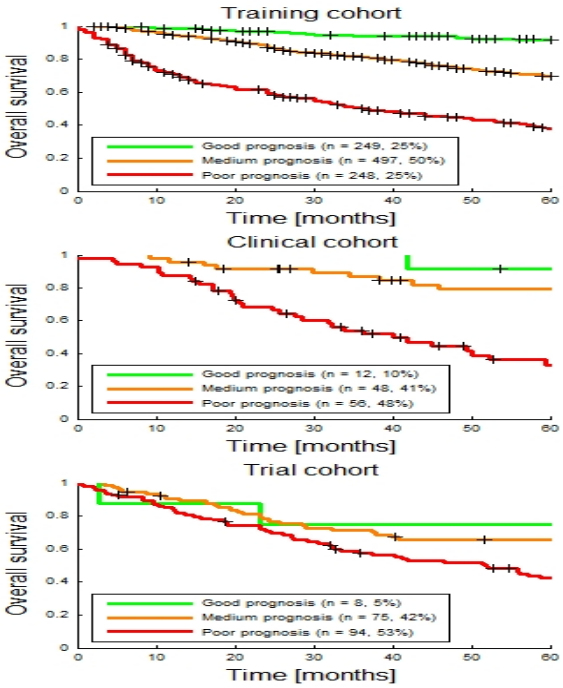

Figure 1: Kaplan Meier survival curves for the training, clinical and trial cohort respectively.

Conclusions: The technical infrastructure and model is able to support the prognosis prediction of laryngeal carcinoma patients in clinical cohort which could be used in future to personalize treatment, improve treatment quality and evaluate these practice changes. The model does not work well for the biased patient population in the trial cohort.

PD-0423

Telomerase: a new target to individualize HNSCC treatment?

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Purpose/Objective: The aim of the studies was to assess the role of telomerase in immortality state of HNSCC cell lines.

Malignant tumors of the head and neck region differs natural clinical outcome and prognosis depending on the histological diagnosis and location. Despite that the diagnostic and therapeutic problems are similar. The gold standard of therapy these tumors, with a view to maximal radicalization of treatment, is combined therapy involving the local (surgery, radiotherapy) and systemic treatment (chemotherapy). Recently, the great interest arouses individualization of cytostatics selection, as well as gene therapy application. One of the targets is telomerase as the enzymatic complex participating in immortality of cancer cells.

Materials and Methods: Knock down of telomerase (TERT subunit) by lentiviral vectors encoding shRNA on cancer cell lines derivated from HNSCC tumors (head and neck cancers are squamous cell carcinoma) and KB cells was carried out. The level of silencing was performed by qPCR and immunofluorescence staining. The impact of drugs (cisplatin and decetaxel) and ionizing radiation on the induction of apoptosis, cell cycle, yH2AX and cell proliferation rate via immunofluorescence staining, cytometer analysis and qPCR was also estimated. The telomere length measurement using a method based on qPCR was assessed.

Results: There was shown an influence of telomerase depletion on apoptosis, proliferation rate and yH2AX expression both in non-treated control cell lines as on cell population after chemoradiotherapy. Moreover, the influence of telomerase knock-down on increased chemo-and radioresistance in vitro was proved.

Conclusions: Our results demonstrate increased chemo- and radiosensitivity in HNSCC cell lines after telomerase silencing. Telomerase is likely to play a pivotal role in chemo- and radioresistance of selected HNSCC cell lines, however further studies are needed.

Poster Discussion: Young Scientists 2: Lung cancer

PD-0424

Immune response profile assessment after stereotactic radiotherapy for lung cancer

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Purpose/Objective: Lung cancer is the most frequent malignant neoplasm with extremely poor prognosis. In earliest stages of the disease clinical benefit of radical surgical excision is similar to stereotactic body radiotherapy (SBRT). The success of high-dose SBRT is certainly related to the X-rays-induced apoptosis. However other, not-well characterized mechanisms may also contribute. We hypothesize that high dose SBRT causes an increase in the expression of multipeptide tumor antigens, which further may lead to a stimulation of specific immune response. Those mechanisms are not fully understood therefore we have designed a prospective study to determine radiation-induced immune response changes. The protocol was approved by Local Ethical Committee.

Objective: to assess the effect of high dose ionizing radiation on changes in the expression of T cell activation markers (CD25, CD28, CTLA-4, PD-1) , transcription factors associated with Th1, Th2, Th17 and regulatory T cell subpopulations of CD4(+) T cells (T-bet, GATA-3, ROR-γt and FoxP3, respectively) in patients treated with SBRT for T1/2N0 M0 NSCLC.

Materials and Methods: Study group consists of patients with newly diagnosed NSCLC stage T1/2N0M0 qualified for SBRT. Patients with comorbidities of significant impact on immune system are excluded. Peripheral blood samples are collected three times from patients: before the treatment (n = 44), 2 weeks (n = 37) and 12 weeks (n = 21) after SRBT. Expression level of selected proteins on peripheral blood lymphocytes is measured by flow cytometry.

Results: The study was started in November 2013. Since then 44 consented patients were included. SBRT was planned and delivered according to the Department's treatment standards. Analysis of blood samples has shown that SRBT significantly increases numbers of PD-1(+) and CTLA-4(+)